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1964
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U.S. National Institutes of Health.
Division of Biological Standards.
Biological products

Public Health Service Publication No. 437
Revised January 1, 1964
Amendment No. 1

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Federal Register
Vol. 30 page 9880
August 7, 1965

TITLE 42--PUBLIC HEALTH
CHAPTER 1--PUBLIC HEALTH SERVICE
DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
SUBCHAPTER F--QUARANTINE
INSPECTION, LICENSING
PART 73--BIOLOGICAL PRODUCTS
ADDITIONAL STANDARDS: ALLERGENIC PRODUCTS

On September 26, 1964, a notice of rule making was published in the Federal Register (29 F.R. 13399) proposing to amend Part 73 of the Public Health Service regulations to include specific standards of safety, purity and potency for the manufacture of Allergenic Products.

Views and arguments respecting the proposed standards were invited to be submitted within 60 days after publication of the notice in the Federal Register, and notice was given of intention to make any amendments that were adopted effective 60 days after the date of their publication in the Federal Register.

After consideration of all comments submitted, the following amendments to Part 73 of the Public Health Service regulations are hereby adopted to become effective 60 days after date of publication in the Federal Register.

Amend Part 73 of the Public Health Service regulations by adding the following to the table of contents at the end thereof:

Additional Standards: Allergenic Products

Sec.

73.500 The product

73.501 Manufacture of Allergenic Products

73.502 Tests

73.503 Dating

Amend Part 73 of the Public Health Service regulations by adding the following at the end thereof:

ADDITIONAL STANDARDS: ALLERGENIC PRODUCTS

§73.500 The product.

(a) Definition. Allergenic Products are products that are administered to man for the diagnosis, prevention or treatment of allergies.

(b) Criteria for source material. Only specifically identified allergenic source materials which contain no more than 1 percent of detectable foreign materials, shall be used in the manufacture of an Allergenic Product. Source materials such as feathers, hairs, and danders shall be free from blood and serum.

§73.501 Manufacture of Allergenic Products.

(a) Extraneous allergenic substances. All manufacturing steps shall be performed so as to insure that the product will contain only the allergenic and other substances intended to be included in the final product.

(b) Cultures derived from microorganisms. Culture media into which organisms are inoculated for the manufacture of Allergenic Products shall contain no allergenic substances other than those necessary as a growth requirement. Neither horse protein nor any allergenic derivative of horse protein shall be used in culture media.

(c) Liquid products for oral administration. Liquid products intended for oral administration that are filled in multiple dose final containers shall contain a preservative in a concentration adequate to inhibit microbial growth.

(d) Residual pyridine. Products for which pyridine is used in manufacturing shall have no more residual pyridine in the final product than 25 micrograms per milliliter.

§73.502 Tests.

(a) Identity. When a specific identity test meeting the provisions of §73.75 cannot be performed, the manufacture of each lot shall be separated from the manufacture of other products in a manner that will preclude adulteration, and records made in the course of manufacture shall be in sufficient detail to verify the identity of the product.

(b) Safety. A safety test shall be performed on the contents of a final container of each lot of each product as prescribed in §73.72 except for the following:

(1) For lots consisting of no more than 20 final containers or 20 sets of individual dilutions, or where the final container contains no more than one intended human dose, the safety test need not be performed on the contents of a final container provided the safety test is performed on each lot of stock concentrate and on each lot of diluent contained in the final product. Only stock concentrates and diluents which have passed the general safety test shall be kept in the work areas used for the manufacture of Allergenic Products. A stock concentrate is an extract derived from a single allergenic source and used in the manufacture of more than one lot of product, and from which final dilutions or mixtures are prepared directly.

(2) For powders for scratch tests, a sample shall be suspended

in a suitable diluent and injected into each animal, and the sample size shall be the single human dose recommended.

(c) Sterility. A sterility test shall be performed on each lot of each Allergenic Product as prescribed in §73.73, with the following exceptions:

(1) When bulk material is not prepared, the sterility test prescribed for bulk material shall be performed on each container of each stock concentrate at the time a stock concentrate is prepared, and the test sample shall be no less than 1 ml. from each stock concentrate container.

(2) For lots consisting of no more than 5 final containers, the final container test shall be performed in accordance with §73.73(f)(7) using the sample therein prescribed or using a sample of no less than 0.25 ml. of product from each final container, divided in approximately equal proportions for testing in Fluid Thioglycollate and Fluid Sabouraud's media. The test sample in the latter alternative method may be an overfill in the final container.

(3) For products prepared in sets of individual dilution series, a test sample of 0.25 ml. shall be taken from a final container of each dilution, which samples may be pooled and one half of the pooled material used for the test with fluid Thioglycollate medium and one-half used for the test with fluid Sabouraud's medium.

(4) Tablets and capsules need not be tested for sterility provided aseptic techniques are employed in their manufacture.

§73.503 Dating.

(a) Periods of cold storage. Allergenic Products may be held

by the manufacturer in cold storage after the date of manufacture without decreasing the dating periods prescribed in paragraph (b) of this section, as follows:

(1) Products with 50 percent or more glycerin and freeze-dried products, at not above 5 degrees C. for three years.

(2) Products with less than 50 percent glycerin, at not above 5 degrees C. for eighteen months.

(b) Dating periods. The dating periods for Allergenic Products shall not exceed the following:

(1) Products with 50 percent or more of glycerin, three years, provided labeling recommends storage from 2 degrees C. to 8 degrees C.

(2) Products with less than 50 percent glycerin, eighteen months, provided labeling recommends storage from 2 degrees C. to 8 degrees C.

(3) Liquid products for which refrigerator temperatures are inappropriate, eighteen months, provided labeling recommends storage at not above 30 degrees C. §73.84 and paragraph (a) of this section do not apply.

(4) Powders and tablets: Five years, provided labeling recommends storage at not above 30 degrees C. §73.84 and paragraph (a) of this section do not apply.

(5) Freeze-dried products: Five years provided labeling recommends storage from 2 degrees C. to 8 degrees C.

Authority: (The provisions of §§73.500 to 73.503 issued under Sec. 215, 58 Stat. 690, as amended; 42 U.S.C. 216. Interpret or apply Sec. 351, 58 Stat. 702; 42 U.S.C. 262).

Dated: July 20, 1965.

Luther L. Terry,
Surgeon General.

Approved: August 3, 1965.

Wilbur J. Cohen,
Acting Secretary.



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